Cell Stem Cell
Obituary

Paolo Bianco (1955–2015)

On November 7, 2015, Prof. Paolo Bianco, a trailblazer in the fields of bone and stem cell biology, and a leading advocate for the ethical development and use of cell-based therapies, was abruptly taken away from us. Paolo will be remembered as a man of enormous intellect and incredible curiosity, with an uncanny ability to "connect the dots" in any problem that caught his interest. He was a true gentleman and friend to all who knew him, with a keen wit and sense of humor. His passing is devastating to his family, his colleagues and friends, the scientific community at large, and the public he served.

Paolo grew up in Lecce, Italy, and fondly recounted his days of being just a boy with his dog and a bicycle, roaming the streets, soaking up his surroundings, and making his dear mother worry. He received his medical training at Sapienza University of Rome, was board certified in anatomic pathology in 1982, and was a full professor at Sapienza at the time of his death.

During his training, his passion for unraveling the causes of disease emerged, and he cultivated a particular interest in the bone/marrow organ, a pursuit that continued throughout his life. Encouraged by his first mentor, Antonio Ascenzi, he delved into the mysteries of bone. True to his nature, he sought to conquer bone, and did a fellowship with Alan Boyde (UCL) to harness the power of computer-driven image analysis using various forms of microscopy (Boyde et al., 1984). In the late 1980s, he joined John Termine's group at the NIH, where he systemically evaluated the expression of bone-enriched proteins by various cells in skeletal and non-skeletal tissues (Bianco et al., 1990, 1991), studies that were quite novel at the time and are still highly cited.

But even before that, Paolo was deeply immersed in gaining a better understanding of the development and cell biology of bone and marrow. He was an early devotee of the work of Alexander Friedenstein and Maureen Owen, who first proposed that bone marrow contains non-hematopoietic stem/progenitor cells responsible for replenishing bone tissue and supporting hematopoiesis (bone marrow stromal cells, or BMSCs, also known as bone-marrow-derived "mesenchymal stem cells"). In his laboratory, and often in collaboration with Pamela Robey (NIH) over the years, he built upon Friedenstein's and Owen's early work, and he rigorously determined for the first time that "skeletal stem cells" (SSCs, a term that he coined) are both multipotent and self-renewing (Sacchetti et al., 2007), the classic definition of a stem cell, and that they are a major contributor to the hematopoietic stem cell niche (Bianco, 2011). Importantly, he strived to bring clarity to the mesenchymal stem cell field by defining in crystal-clear terms what they are, what they are not, and what they can and cannot do (Bianco et al., 2013b).

Along the way, Paolo recognized the central role of SSCs/BMSCs in mediating bone homeostasis, leading him to hypothesize that genetic mutations that affect the function of these cells could result in skeletal disease. Proof of principle came with his seminal studies on fibrous dysplasia of bone (FD) caused by mutations in *GNAS* (coding for Gsα). He showed that in vivo transplantation of mutated SSCs/BMSCs regenerated an abnormal ectopic ossicle fully reminiscent of lesional bone (Bianco et al., 1998). He dedicated a large part of the last 15 years to dissecting out the pathogenetic mechanisms of FD. Through the generation of the first mouse model of FD (Saggio et al., 2014) and other models, he was hot on the trail to identify which specific cell in the bone/marrow microenvironment is the culprit, work that is being continued by his long-time colleague, Mara Riminucci.

The microscope was Paolo's window to the world, and he was never happier than when looking down the tube or at a histological image. Without a doubt, he was *the* expert in interpreting the histology and histopathology of bone and associated tissues. He would often turn away from the scope, with a cigarette in hand, clouded in smoke, a twinkle in his eyes, and a very special smile on his face, and say, "Hey, come look at this! I've figured it out." Along with his deep understanding of development and cell and molecular biology, he, along with many collaborators (too numerous to list here), made countless contributions to many fields.

Paolo Bianco
Paolo at a meeting in Chengdu, China in 2011.

As much as he was a great scientist, Paolo was a beloved teacher, mentor, and communicator, as witnessed by his numerous appointments at Sapienza and his affiliations with other institutions as a Ph.D. advisor and in other capacities. Sitting in on his classes, or at his presentations given around the world, was a captivating experience. Whether in Italian or English, his command of language was astounding; with just the right words, he spoke with such enthusiasm that one could not help but be totally enthralled. His students were often in his office, and they very much appreciated that they were being taught and trained by a true scholar. At the memorial ceremony held for Paolo at Sapienza, students and faculty alike flocked into the chapel and poured out into the street in order to pay their last respects to their dear teacher and colleague.

His contributions as an educator and champion of science were not limited to the classroom; he will also be remembered as one of the most vigorous

skeptics of the Stamina Foundation, an organization that gained widespread attention in Italy and internationally for the reckless therapeutic claims it made about a supposed stem cell therapy—claims that Paolo and his colleagues Elena Cattaneo and Michele De Luca were among the first to call into question. For Paolo, the Stamina incident came to represent a broader danger, challenging the integrity of biomedical practice (Bianco et al., 2013a). With his characteristic energy and rigor, he had dedicated much of his time over the past several years to uncovering the root causes of this phenomenon and advocating for systemic reforms to support what he saw as an embattled scientific enterprise (Bianco and Sipp, 2014).

Paolo's work, which extended into many areas, was his life; his life was his work. He was a voracious reader, worked too hard, traveled too much, smoked like a chimney, and ran a busy pathology diagnostic service. He ranted and raved when his high standards demanded that he do so, but he always voiced his defense for the good of science and the public. He was a truly good soul. He juggled many things in his life, but he would not have done it any other way. He will be sorely missed.

Let us not forget Paolo, and let us continue to work with his vision in our minds and his spirit in our hearts. That is what he would want, and these are the best ways to honor him.

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